

L Number	Hits	Search Text	DB	Time stamp
1	3794	quinazolin or quinazolinyl	USPAT; US-PGPUB	2002/10/24 16:33
2	7745	quinolin or quinolinyl	USPAT; US-PGPUB	2002/10/24 16:33
3	9749	(quinazolin or quinazolinyl) or (quinolin or quinolinyl)	USPAT; US-PGPUB	2002/10/24 16:33
4	500	((quinazolin or quinazolinyl) or (quinolin or quinolinyl)) and (allenylene or vinylene or ethynylene or butadien)	USPAT; US-PGPUB	2002/10/24 16:34
5	469	((quinazolin or quinazolinyl) or (quinolin or quinolinyl)) and (allenylene or vinylene or ethynylene or butadien)) and amino	USPAT; US-PGPUB	2002/10/24 16:35

EAST

9/914,323

09/ 914,323

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Apr 08	"Ask CAS" for self-help around the clock
NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
NEWS	11	Jun 10	PCTFULL has been reloaded
NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS	14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS	15	Jul 30	NETFIRST to be removed from STN
NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	18	Aug 08	NTIS has been reloaded and enhanced
NEWS	19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS	21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS	22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	23	Sep 03	JAPIO has been reloaded and enhanced
NEWS	24	Sep 16	Experimental properties added to the REGISTRY file
NEWS	25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS	26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	28	Oct 21	EVENTLINE has been reloaded
NEWS EXPRESS			October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

09/ 914,323

FILE 'HOME' ENTERED AT 16:25:32 ON 24 OCT 2002

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 16:25:40 ON 24 OCT 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 OCT 2002 HIGHEST RN 464874-85-9

DICTIONARY FILE UPDATES: 23 OCT 2002 HIGHEST RN 464874-85-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 09914323.str

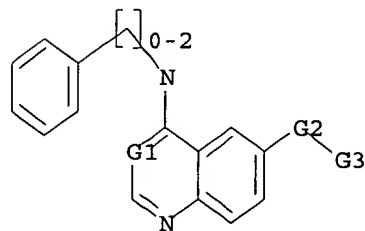
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

10



G1 C,N

G2 O,N

G3 SO2, [01]

09/ 914,323

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 16:26:18 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1447 TO ITERATE

69.1% PROCESSED 1000 ITERATIONS 42 ANSWERS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 26659 TO 31221

PROJECTED ANSWERS: 748 TO 1682

L2 42 SEA SSS SAM L1

=> s l1 ful

FULL SEARCH INITIATED 16:26:25 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 28557 TO ITERATE

100.0% PROCESSED 28557 ITERATIONS 1020 ANSWERS  
SEARCH TIME: 00.00.04

L3 1020 SEA SSS FUL L1

=> s l3 and (allenyl? or vinyl? or butadien? or ethynyl?)

202 ALLENYL?

65374 VINYL?

45326 BUTADIEN?

81398 ETHYNYL?

L4 19 L3 AND (ALLENYL? OR VINYL? OR BUTADIEN? OR ETHYNYL?)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
157.42	157.63

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 16:28:14 ON 24 OCT 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 24 Oct 2002 VOL 137 ISS 17

FILE LAST UPDATED: 23 Oct 2002 (20021023/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please

09/ 914,323

check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l4

L5 9 L4

=> d l5 1- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:658094 CAPLUS

DOCUMENT NUMBER: 137:185509

TITLE: Preparation of 4-phenylaminoquinazoline derivatives as inhibitors of tyrosine-specific protein kinase

INVENTOR(S): Kitano, Yasunori; Kawahara, Eiji; Suzuki, Tsuyoshi; Abe, Daisuke; Nakajou, Masahiro; Ueda, Naoko

PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan

SOURCE: PCT Int. Appl., 154 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066445	A1	20020829	WO 2002-JP1575	20020221
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			JP 2001-45827	A 20010221
			JP 2001-353525	A 20011119
OTHER SOURCE(S):	MARPAT 137:185509			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Compds. represented by the following general formula (I) or pharmaceutically acceptable salts thereof, hydrates or solvates of the same or mixts. of optically active isomers, racemic compds. or diastereomers of the same [n = an integer of 0-3; R1 = H, halo, HO, cyano, NO2, CF3, C1-5 alkyl, C1-5 alkoxy, S(O)f-C1-5 alkyl (wherein f = an integer of 0-2), (un)substituted NH2; one of R2 and R2 is R27SO2NH, (R28SO2)2N, C1-5 alkoxy, MeCOCH2CONH, MeSCH2CH2OCONH, or NCCH2CONH, etc. (wherein R27, R28 = optionally morpholino-substituted C1-5 alkyl) and the other one represents Y(CR12R13)mCR8R9C.tplbond.C, Y(CR12R13)mCR8R9CH:CH, Q, Q1 (wherein R8, R9 = H, optionally HO- or C1-5 alkoxy substituted C1-5 alkyl, or CR8 R9 together represent C0 or C3-8 cycloalkylene optionally interrupted by O, S, NH, or alkyl-N; Y = H, HO, C1-5 alkoxy, C1-5 alkanoyloxy, etc.; R11, R12 = H, C1-5 alkyl; m = an integer of 0-3; p, q = 2,3; Z = O, S, SO, SO2, CO, optionally substituted NH; p1, p2 = an integer of 1-3; n1 = 0,1; W = H, HO, C1-5 alkoxy, C1-5 alkanoyloxy, CO2H, cyano, di-C1-5 alkyamino, morpholino, etc.]] are prepd. These compds. have an

excellent protein kinase inhibitory activity specific to tyrosine and, therefore, are usable as drugs, in particular, remedies/preventives for various cancers, diseases caused by arteriosclerosis or psoriasis. Thus, 1-(1,1-dimethyl-2-propynyl)-4-methylpiperazine was treated with 4,4,5,5-tetramethyl-1,3,2-dioxaborane in the presence of  $\text{PhCl}(\text{PPh}_3)_3$  in THF/ $\text{CH}_2\text{Cl}_2$  at room temp. and coupled with 4-(3-chloro-4-fluorophenylamino)-6-methoxy-7-quinazolinyl triflate (prepn. given) in the presence of  $\text{PdCl}_2(\text{dppf}) \cdot \text{CH}_2\text{Cl}_2$  [dppf = 1,1'-bis(diphenylphosphino)ferrocene] in a mixt. of DMF and 2 m aq.  $\text{Na}_2\text{CO}_3$  80.degree. for 1 h to give the title compd. (II). II.HCl showed  $\text{IC}_{50}$  of 0.82 nM against EGF receptor tyrosine kinase.

IT 451493-01-9P 451494-03-4P 451494-18-1P  
451494-25-0P

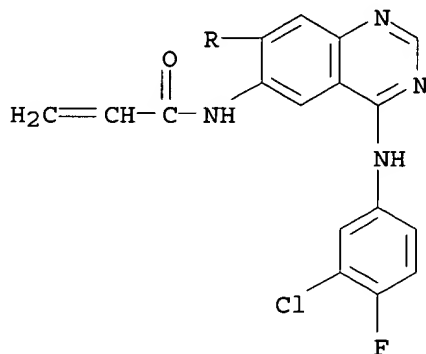
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for prepn. and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

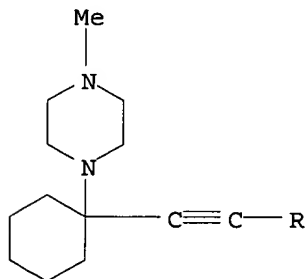
RN 451493-01-9 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[1-(4-methyl-1-piperazinyl)cyclohexyl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

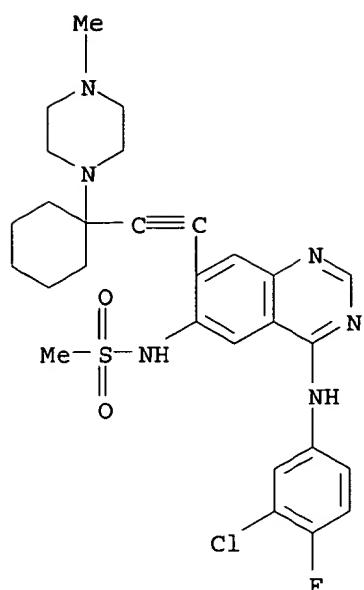


PAGE 2-A



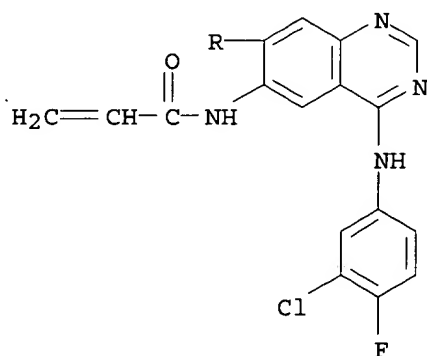
RN 451494-03-4 CAPLUS

CN Methanesulfonamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[1-(4-methyl-1-piperazinyl)cyclohexyl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

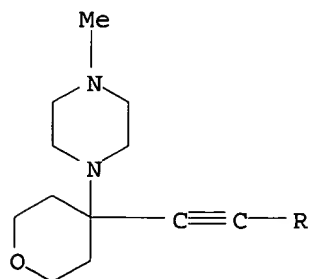


RN 451494-18-1 CAPLUS  
 CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[tetrahydro-4-(4-methyl-1-piperazinyl)-2H-pyran-4-yl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RN 451494-25-0 CAPLUS  
 CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[4-(diethylamino)-2H-pyran-4-yl]ethynyl]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

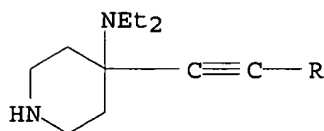
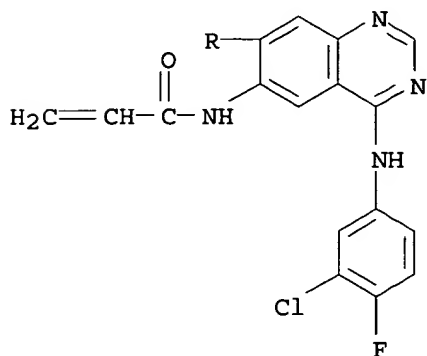
09/ 914,323

4-piperidinyl]ethynyl]-6-quinazolinyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 451494-24-9

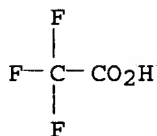
CMF C28 H30 Cl F N6 O



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 451494-23-8P

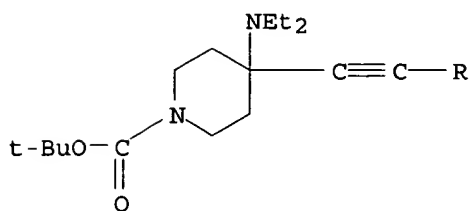
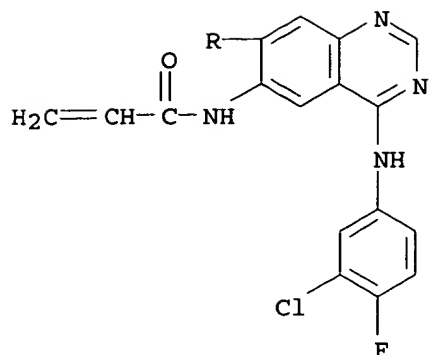
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for prepn. and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

RN 451494-23-8 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[4-[(3-chloro-4-fluorophenyl)amino]-6-[(1-oxo-2-propenyl)amino]-7-quinazolinyl]ethynyl]-4-(diethylamino)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693148 CAPLUS

DOCUMENT NUMBER: 135:242152

TITLE: Preparation of 4-anilinoquinoline-3-carbonitriles as colonic polyp inhibitors

INVENTOR(S): Frost, Philip; Discafani-Marro, Carolyn M.

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 207 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068186	A2	20010920	WO 2001-US7068	20010306
WO 2001068186	A3	20020117		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

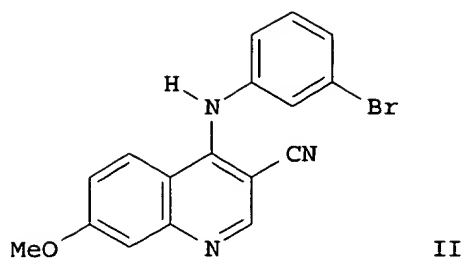
US 6384051 B1 20020507 US 2001-805070 20010313

PRIORITY APPLN. INFO.: US 2000-304198P P 20000313

US 2000-524196 A 20000313

OTHER SOURCE(S): MARPAT 135:242152

GI



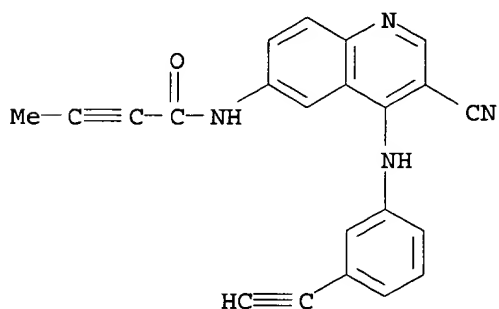
AB R(CH<sub>2</sub>)<sub>n</sub>ZZ1CN [I; R = (un)substituted cycloalkyl, -Ph, -pyridinyl, -pyrimidinyl; Z = O, S, (alkyl)imino; Z1 = 5-8-(un)substituted quinoline-4,3-diyl; n = 0 or 1] were prepd. Thus, 3-(MeO)C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> was cyclocondensed with NCC(:CHOEt)CO<sub>2</sub>Et and the chlorinated product aminated by 3-BrC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> to give title compd. II. Data for biol. activity of 1 prepd. I were given.

IT 214485-23-1P 214485-24-2P 214485-25-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of 4-anilinoquinoline-3-carbonitriles as colonic polyp inhibitors)

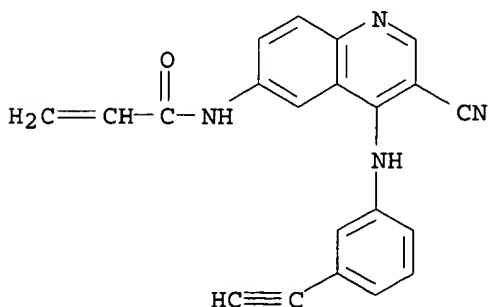
RN 214485-23-1 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl] - (9CI)  
(CA INDEX NAME)



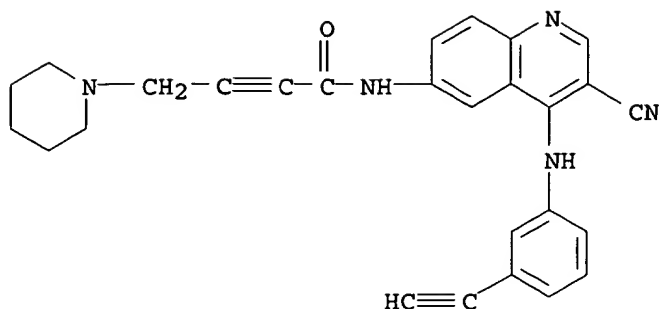
RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl] - (9CI)  
(CA INDEX NAME)



RN 214485-25-3 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-piperidinyl) - (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:185 CAPLUS

DOCUMENT NUMBER: 134:207783

TITLE: Tyrosine kinase inhibitors. 18. 6-Substituted 4-anilinoquinazolines and 4-anilinopyrido[3,4-d]pyrimidines as soluble, irreversible inhibitors of the epidermal growth factor receptor

AUTHOR(S): Smaill, Jeff B.; Showalter, H. D. Hollis; Zhou, Hairong; Bridges, Alexander J.; McNamara, Dennis J.; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Vincent, Patrick W.; Roberts, Bill J.; Elliott, William L.; Denny, William A.

CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 429-440  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,4-d]pyrimidine-6-acrylamides are potent pan-erbB tyrosine kinase inactivators, and one example (CI-1033) is in clin. trial. A series of analogs with a variety of Michael acceptor units at the 6-position, I [X = N, C, R1 = H, Me, (CH2)2NMe2, etc., R2 = H, Me, R3 = H, cis-Cl, CF3, etc.], II, and III (X = N, C, R1 = NHSO2CH:CH2, SO2CH2CH2OH, SO2CH:CH2, SOCH:CH2), were prepd. to define the structural requirements for irreversible inhibition. A particular goal was to det. whether addnl. functions to increase soly. could be appended to the Michael acceptor. Substituted acrylamides were prepd. by direct acylation of the corresponding 6-amines with the requisite acid or acid chloride. Vinylsulfonamide derivs. were obtained by acylation of the amines with chloroethylsulfonyl chloride followed by base-promoted elimination. Vinylsulfone and vinylsulfine derivs. were prepd. by oxidn. and base elimination of a hydroxyethylthio intermediate. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Substitution at the nitrogen of the acrylamide was tolerated only with a Me group; larger substituents were dystherapeutic, and no substitution at all was tolerated

at the acrylamide .alpha.-carbon. In contrast, while electron-donating groups at the acrylamide .beta.-carbon were not useful, even quite large electron-withdrawing groups (which increase its electrophilicity) were tolerated. A series of derivs. with soly.-enhancing substituents linked to the acrylamide .beta.-carbon via amides were potent irreversible inhibitors of isolated EGFR (IC50s = 0.4-1.1 nM), with weakly basic morpholine and imidazole derivs. being the best. Vinylsulfonamides were also potent and irreversible inhibitors, but vinylsulfones and vinylsulfines were reversible and only poorly active. Two compds. were evaluated against A431, H125, and MCF-7 xenografts in nude mice but were inferior in these assays to the clin. trial compd. CI-1033.

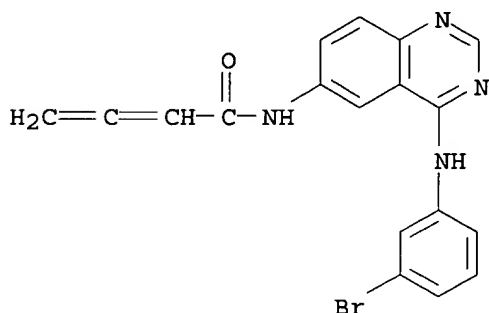
IT 198960-23-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn., epidermal growth factor receptor inhibitory activity, and structure-activity relationship of anilinoquinazolines and -pyridopyrimidines)

RN 198960-23-5 CAPLUS

CN 2,3-Butadienamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:794373 CAPLUS

DOCUMENT NUMBER: 132:35620

TITLE: Preparation of substituted 3-cyanoquinolines as inhibitors of growth factor receptor protein tyrosine kinases (PTK)

INVENTOR(S): Wissner, Allan; Johnson, Bernard D.; Reich, Marvin F.; Floyd, Middleton B., Jr.; Kitchen, Douglas B.; Tsou, Hwei-ru

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: U.S., 80 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

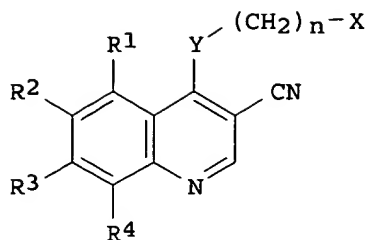
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

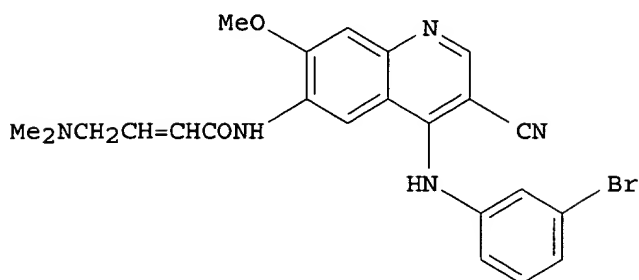
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6002008	A	19991214	US 1998-49718	19980327
PRIORITY APPLN. INFO.:			US 1997-41963P	P 19970403
OTHER SOURCE(S):		MARPAT 132:35620		

GI



I



II

AB This invention provides compds. having the formula (I; wherein: X is cycloalkyl which may be optionally substituted; or is a pyridinyl, pyrimidinyl, or Ph ring; wherein the pyridinyl, pyrimidinyl, or Ph ring may be optionally substituted; n is 0-1; Y is NH, O, S, or NR; R is alkyl of 1-6 carbon atoms; R1, R2, R3, and R4 are each, independently, hydrogen, halogen, alkyl, alkenyl, alkynyl, alkenyloxy, alkynoyloxy, hydroxymethyl, halomethyl, alkanoyloxy, alkenoyloxy, alkynyloxy, alkanoyloxymethyl, alkenoyloxymethyl, alkynoyloxymethyl, alkoxymethyl, alkoxy, alkylthio, alkylsulphanyl, alkylsulfonyl, alkylsulfonamido, alkenylsulfonamido, alkynylsulfonamido, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy, carboalkyl, phenoxy, Ph, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino, alkylamino, dialkylamino, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, phenylamino, benzylamino, etc.; R5 is alkyl which may be optionally substituted, or Ph which may be optionally substituted; R6 is hydrogen, alkyl, or alkenyl; R7 is chloro or bromo; R8 is hydrogen, alkyl, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, N-cycloalkylaminoalkyl, N-cycloalkyl-N-alkylaminoalkyl, N,N-dicycloalkylaminoalkyl, morpholino-N-alkyl, piperidino-N-alkyl, N-alkyl-piperidino-N-alkyl, azacycloalkyl-N-alkyl, hydroxyalkyl, alkoxyalkyl, carboxy, carboalkoxy, Ph, carboalkyl, chloro, fluoro, or bromo; Z is amino, hydroxy, alkoxy, alkylamino, dialkylamino). The compds. of the present invention inhibit the action of certain growth factor receptor protein tyrosine kinases (PTK) thereby inhibiting the abnormal growth of certain cell types. They are therefore useful for the treatment of certain diseases that are the result of deregulation of these PTKs, in particular as anti-cancer agents for the treatment of cancers expressing epidermal growth factor receptor (EGFR), mitogen activated protein kinase (MAPK), epithelial kinase (ECK), and kinase insert domain contg. receptor (KDR) in mammals and for the treatment of polycystic kidney disease in mammals. Thus, To a mixt. of 1.9 g (5.1 mmol) of 4-[(3-bromophenyl)amino]-7-methoxy-6-amino-3-quinolinecarbonitrile and 5.3 mL (31 mmol) of Hunig's base in 110 mL of dry THF at 0.degree. C., with stirring, was added a THF soln. contg. 5.7 g (31 mmol) of 4-bromocrotonyl chloride dropwise. The mixt. was stirred for addnl. 0.5 h. After addn. 100 mL of satd. sodium chloride soln. was added to the reaction mixt., then it was extd. with Et acetate. The Et acetate soln. was dried over

sodium sulfate and then was added to 40 mL of di-Me amine soln. (2.0 M in THF) at 0.degree. dropwise and stirred an addnl. 0.5 h to give 4-Dimethylamino-but-2-enoic acid [4-(3-bromo-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]amide (II). II showed IC<sub>50</sub> of 0.000008 .mu.M against epidermal growth factor receptor kinase.

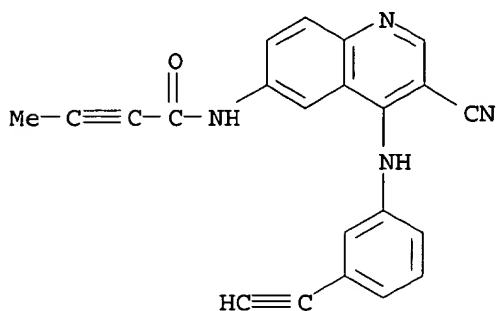
IT 214485-23-1P 214485-24-2P 214485-25-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted 3-cyanoquinolines as inhibitors of growth factor receptor protein tyrosine kinases (PTK) for treatment of cancers and polycystic kidney disease)

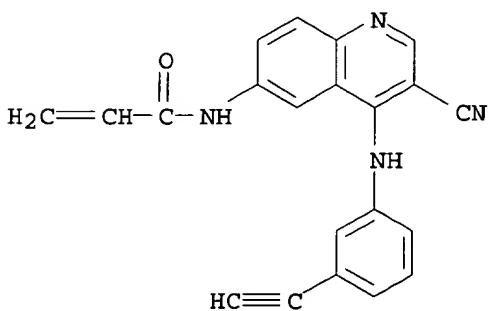
RN 214485-23-1 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI)  
(CA INDEX NAME)



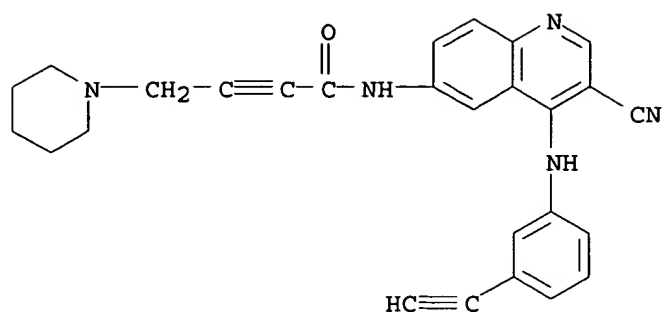
RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]- (9CI)  
(CA INDEX NAME)



RN 214485-25-3 CAPLUS

CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:113656 CAPLUS

DOCUMENT NUMBER: 130:168387

TITLE: Irreversible inhibitors of tyrosine kinases

INVENTOR(S): Bridges, Alexander James

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906378	A1	19990211	WO 1998-US15784	19980729
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9887607	A1	19990222	AU 1998-87607	19980729
US 6127374	A	20001003	US 1999-269545	19990325
PRIORITY APPLN. INFO.:			US 1997-54060P	P 19970729
			WO 1998-US15784	W 19980729

OTHER SOURCE(S): MARPAT 130:168387

AB Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH<sub>2</sub>OH was treated with 4-FC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub> to give 4-PhCH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzoyloxylanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzoyloxylanilino)quinazolin-6-yl]acrylamide (I). I had an IC<sub>50</sub> for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.

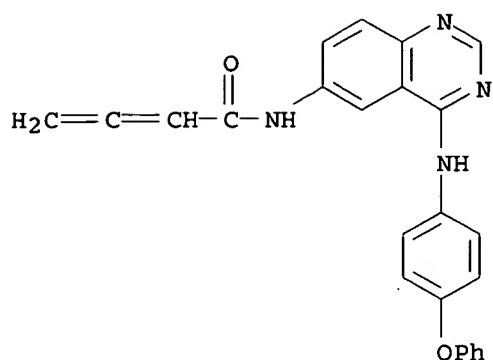
IT 220488-36-8P 220488-37-9P 220489-67-8P  
220489-69-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of anilinoquinazolinylacrylamides and related compds. as tyrosine kinase inhibitors)

RN 220488-36-8 CAPLUS

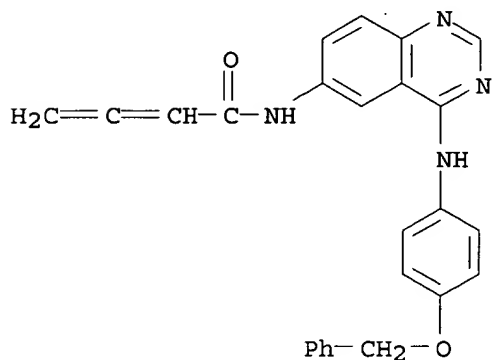
CN 2,3-Butadienamide, N-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI)  
(CA INDEX NAME)

09/ 914,323



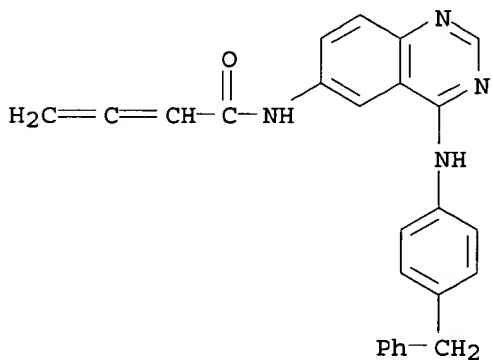
RN 220488-37-9 CAPLUS

CN 2,3-Butadienamide, N-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]-  
(9CI) (CA INDEX NAME)



RN 220489-67-8 CAPLUS

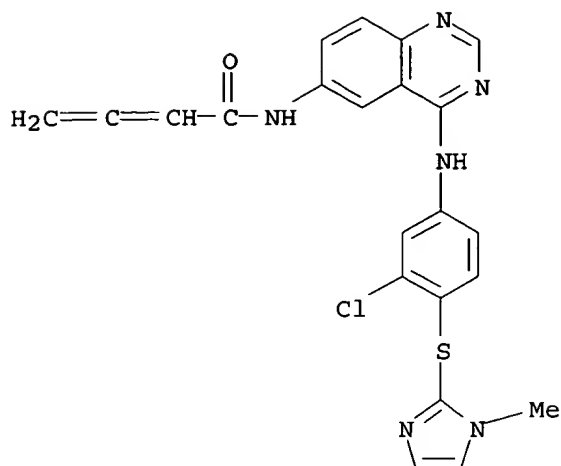
CN 2,3-Butadienamide, N-[4-[[4-(phenylmethyl)phenyl]amino]-6-quinazolinyl]-  
(9CI) (CA INDEX NAME)



RN 220489-69-0 CAPLUS

CN 2,3-Butadienamide, N-[4-[[3-chloro-4-[(1-methyl-1H-imidazol-2-yl)thio]phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:682233 CAPLUS

DOCUMENT NUMBER: 129:302564

TITLE: Preparation of substituted 3-cyanoquinolines as inhibitors of protein tyrosine kinase

INVENTOR(S): Wissner, Allan; Johnson, Bernard Dean; Reich, Marvin Fred; Floyd, Middleton Brawner, Jr.; Kitchen, Douglas B.; Tsou, Hwei-ru

PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: PCT Int. Appl., 223 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

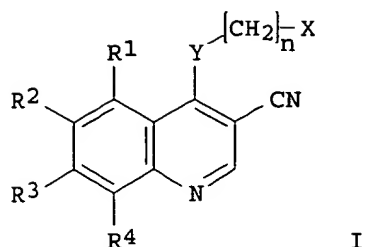
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843960	A1	19981008	WO 1998-US6480	19980402
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CN 1161330	A	19971008	CN 1997-101099	19970204
ZA 9802771	A	19991001	ZA 1998-2771	19980401
AU 9868777	A1	19981022	AU 1998-68777	19980402
AU 750906	B2	20020801		
EP 973746	A1	20000126	EP 1998-914417	19980402
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
JP 2001519788	T2	20011023	JP 1998-541981	19980402
NO 9904798	A	19991124	NO 1999-4798	19991001
PRIORITY APPLN. INFO.:			US 1997-826604	A 19970403
			WO 1998-US6480	W 19980402

OTHER SOURCE(S): MARPAT 129:302564

GI



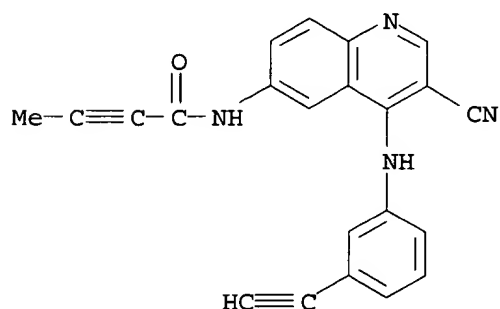
AB The title compds. [I; X = (un)substituted cycloalkyl, pyridinyl, pyrimidinyl, Ph; n = 0-1; Y = NH, O, S, NR; R = C1-6 alkyl; R1-R4 = H, halo, alkyl, etc. (with the proviso that when Y = NH; R1-R4 = H; n = 0; X is not 2-methylphenyl)], inhibitors of protein tyrosine kinase which are useful in treating, inhibiting the growth of, or eradicating a neoplasm which expresses EGFR, MAPK, ECK or KDR, and in treating polycystic kidney disease, were prepd. Thus, treatment of 2-butyric acid with iso-Bu chloroformate and N-methylmorpholine in THF followed by the addn. of this soln. of the mixed anhydride to a soln. of 6-amino-4-[(3-bromophenyl)amino]-7-methoxy-3-quinolinecarbonitrile (prepn. described) in THF over a 24 h period afforded I [Y = NH; n = 0; X = 3-BrC<sub>6</sub>H<sub>4</sub>; R1 = R4 = H; R2 = MeC.tplbond.CC(O)NH; R3 = MeO] which showed IC<sub>50</sub> of 0.15 .mu.M against epidermal growth factor receptor kinase (A431 membrane ext.).

IT 214485-23-1P 214485-24-2P 214485-25-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of substituted 3-cyanoquinolines as inhibitors of protein tyrosine kinase)

RN 214485-23-1 CAPLUS

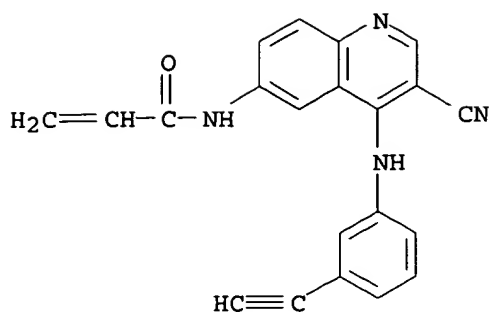
CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl] - (9CI)  
(CA INDEX NAME)



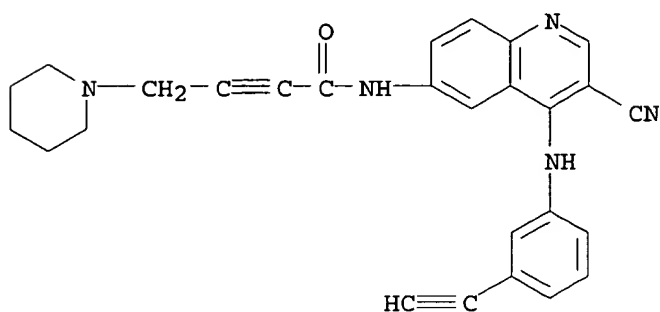
RN 214485-24-2 CAPLUS

CN 2-Propenamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl] - (9CI)  
(CA INDEX NAME)

09/ 914,323



RN 214485-25-3 CAPLUS  
CN 2-Butynamide, N-[3-cyano-4-[(3-ethynylphenyl)amino]-6-quinolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)

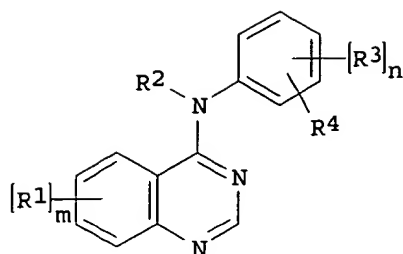


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1998:282401 CAPLUS  
DOCUMENT NUMBER: 128:321653  
TITLE: Preparation of alkynyl- and azido-substituted 4-anilinoquinazolines for the treatment of hyperproliferative diseases  
INVENTOR(S): Schnur, Rodney Caughren; Arnold, Lee Daniel  
PATENT ASSIGNEE(S): Pfizer Inc., USA  
SOURCE: U.S., 23 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5747498	A	19980505	US 1996-653786	19960528

OTHER SOURCE(S): CASREACT 128:321653; MARPAT 128:321653  
GI



I

AB The title compds. [I; R1 = H, halo, OH, etc.; R2 = H, (un)substituted C1-6 alkyl; R3 = H, halo, OH, etc.; R4 = N3, (un)substituted ethynyl; m = 1-3; n = 1-2] and their salts, useful in the treatment of hyperproliferative diseases such as cancer, were prepd. Thus, reaction of 4-chloro-6,7-dimethoxyquinazoline with 4-azidoaniline hydrochloride in iPrOH afforded 98% I [R1 = 6,7-Me2; R2, R3 = H; R4 = 4-N3]. Compds. I showed IC50 of 0.0001-30 .mu.M against EGFR kinase.

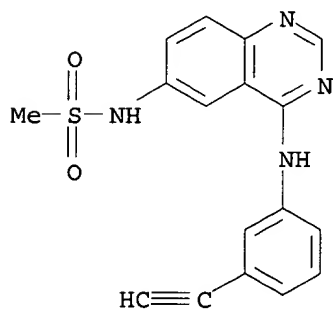
IT 183319-40-6P 183319-48-4P 183319-51-9P  
183321-68-8P 183321-69-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of alkynyl- and azido-substituted 4-anilinoquinazolines for the treatment of hyperproliferative diseases)

RN 183319-40-6 CAPLUS

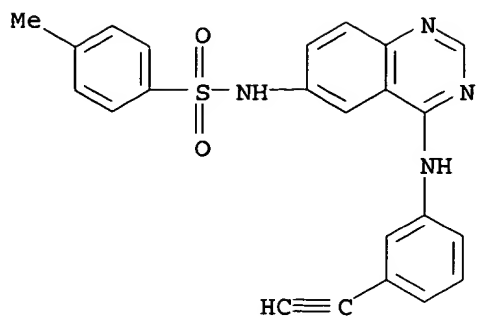
CN Methanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]- (9CI)  
(CA INDEX NAME)



RN 183319-48-4 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

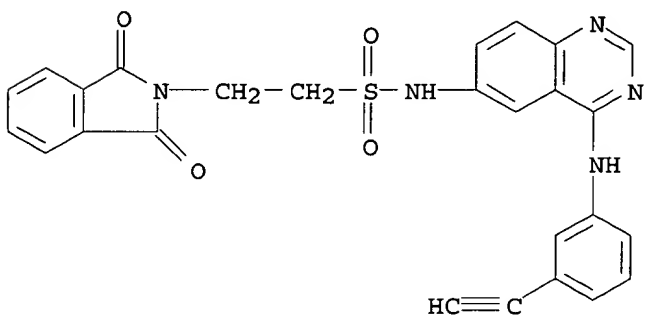
09/ 914,323



● HCl

RN 183319-51-9 CAPLUS

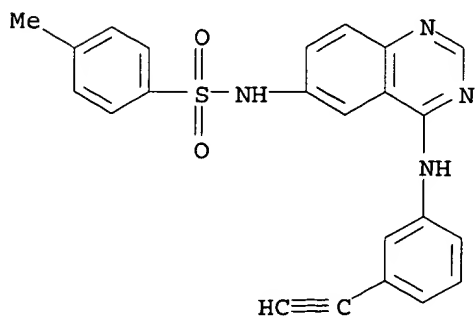
CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

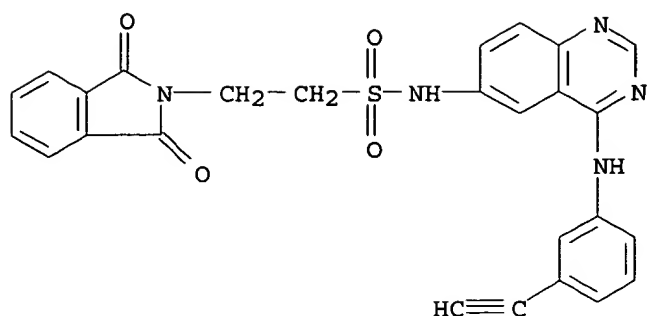
RN 183321-68-8 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-(9CI) (CA INDEX NAME)



RN 183321-69-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:696745 CAPLUS

DOCUMENT NUMBER: 128:3695

TITLE: Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors

INVENTOR(S): Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.

PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong

SOURCE: PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

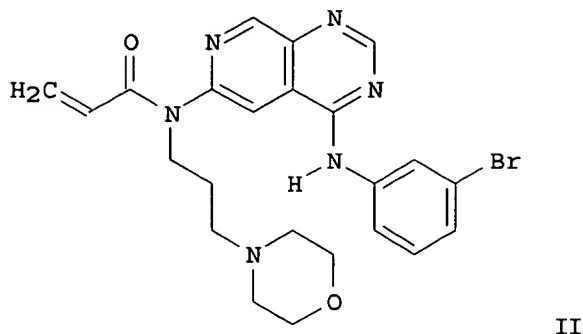
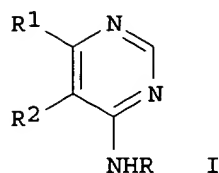
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738983	A1	19971023	WO 1997-US5778	19970408
W:	AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2249446	AA	19971023	CA 1997-2249446	19970408
AU 9724463	A1	19971107	AU 1997-24463	19970408
AU 725533	B2	20001012		
EP 892789	A1	19990127	EP 1997-920213	19970408
EP 892789	B1	20020227		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI			
CN 1218456	A	19990602	CN 1997-194458	19970408
BR 9708640	A	19990803	BR 1997-8640	19970408
JP 2000508657	T2	20000711	JP 1997-537173	19970408
AT 213730	E	20020315	AT 1997-920213	19970408
ZA 9703060	A	19971104	ZA 1997-3060	19970410
NO 9804718	A	19981209	NO 1998-4718	19981009
KR 2000005364	A	20000125	KR 1998-8086	19981010
KR 2000005364	A	20000125	KR 1998-708086	19981010
US 6344459	B1	20020205	US 1999-155501	19990608
PRIORITY APPLN. INFO.:			US 1996-15351P P	19960412

OTHER SOURCE(S) :  
GI

MARPAT 128:3695



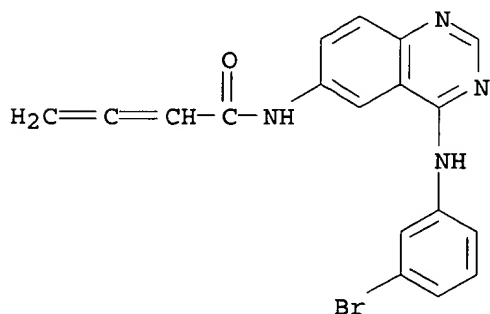
AB Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1Z2R10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinopropanamine and the product acylated by CH2:CHCOCl to give title compd. II. Data for biol. activity of I were given.

IT 198960-23-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors)

RN 198960-23-5 CAPLUS

CN 2,3-Butadienamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:701606 CAPLUS

DOCUMENT NUMBER: 125:328728

TITLE: Preparation of N-phenylquinazoline-4-amines as neoplasm inhibitors

INVENTOR(S) : Schnur, Rodney C.; Arnold, Lee D.

PATENT ASSIGNEE(S) : Pfizer Inc., USA

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630347	A1	19961003	WO 1995-IB436	19950606
W: CA, FI, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2216796	AA	19961003	CA 1995-2216796	19950606
EP 817775	A1	19980114	EP 1995-918713	19950606
EP 817775	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 10506633	T2	19980630	JP 1995-529113	19950606
JP 3088018	B2	20000918	JP 1996-529113	19950606
EP 1110953	A1	20010627	EP 2001-104696	19950606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 205483	E	20010915	AT 1995-918713	19950606
ES 2161290	T3	20011201	ES 1995-918713	19950606
TW 454000	B	20010911	TW 1996-85102699	19960305
CN 1137037	A	19961204	CN 1996-102992	19960328
CN 1066142	B	20010523		
NO 9601299	A	19961001	NO 1996-1299	19960329
AU 9650406	A1	19961010	AU 1996-50406	19960329
AU 703638	B2	19990325		
ZA 9602522	A	19970929	ZA 1996-2522	19960329
BR 9601200	A	19980106	BR 1996-1200	19960329
RU 2174977	C2	20011020	RU 1996-106055	19960329
FI 9703832	A	19970929	FI 1997-3832	19970929
AU 9935854	A1	19990819	AU 1999-35854	19990623

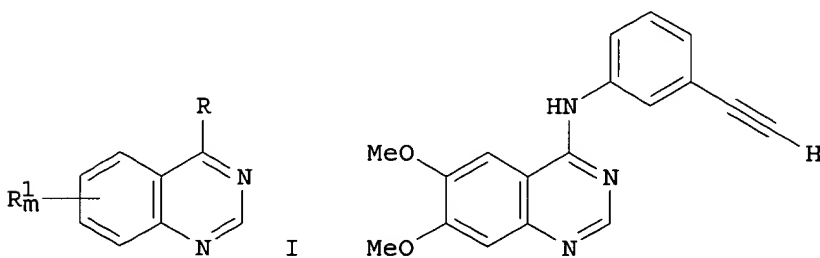
PRIORITY APPLN. INFO.:

US 1995-413300	A2	19950330
EP 1995-918713	A3	19950606
WO 1995-IB436	W	19950606
AU 1996-50406	A3	19960329

OTHER SOURCE(S):

MARPAT 125:328728

GI



AB Title compds. [I; r = NR<sub>2</sub>ZR<sub>4</sub>; R<sub>1</sub> = H, halo, NH<sub>2</sub>, CO<sub>2</sub>H, etc.; R<sub>2</sub> = H (un)substituted alkyl; R<sub>4</sub> = N<sub>3</sub>, C.tplbond.CR<sub>3</sub>; R<sub>3</sub> = H, (un)substituted alkyl; Z = (un)substituted phenylene; m = 1-3] were prepd. Thus, 4-chloro-6,7-dimethoxyquinazoline was aminated by 3-(HC.tplbond.C)C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> to give title compd. II. I had IC<sub>50</sub> of 10<sup>-4</sup> to 30.μM against phosphorylation on Lys3-gastrin tyrosine by epidermal growth factor receptor kinase in vitro.

IT 183319-40-6P 183319-48-4P 183319-51-9P  
183321-68-8P 183321-69-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

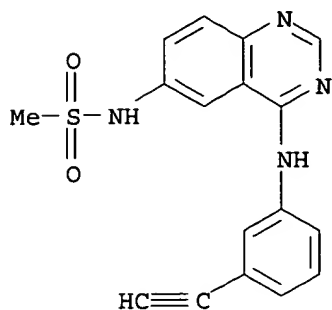


09/ 914,323

BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of N-phenylquinazoline-4-amines as neoplasm inhibitors)

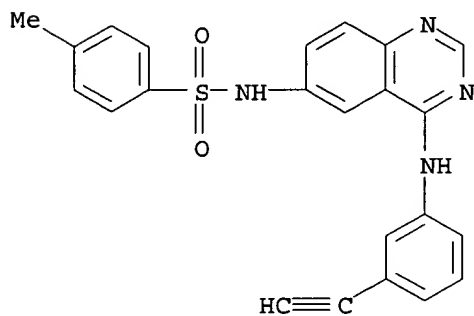
RN 183319-40-6 CAPLUS

CN Methanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]- (9CI)  
(CA INDEX NAME)



RN 183319-48-4 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

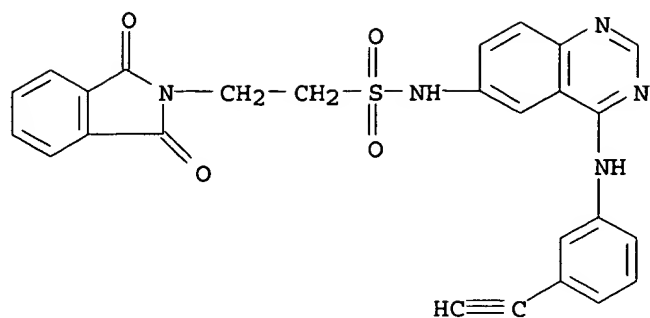


● HCl

RN 183319-51-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

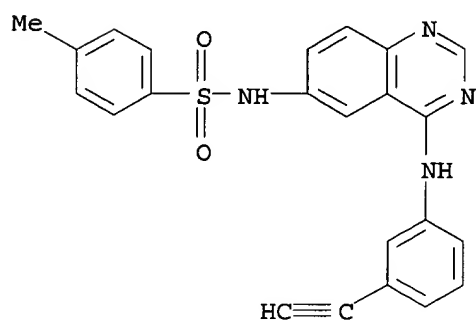
09/ 914,323



● HCl

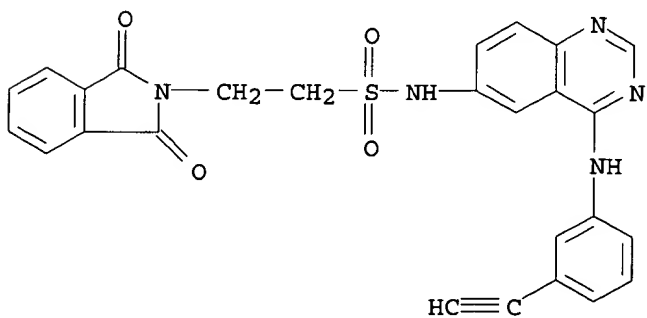
RN 183321-68-8 CAPLUS

CN Benzenesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-4-methyl-  
(9CI) (CA INDEX NAME)



RN 183321-69-9 CAPLUS

CN 2H-Isoindole-2-ethanesulfonamide, N-[4-[(3-ethynylphenyl)amino]-6-quinazolinyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 16:25:32 ON 24 OCT 2002)

FILE 'REGISTRY' ENTERED AT 16:25:40 ON 24 OCT 2002

L1 STRUCTURE UPLOADED

L2 42 S L1

09/ 914,323

L3 1020 S L1 FUL

L4 19 S L3 AND (ALLENYL? OR VINYL? OR BUTADIEN? OR ETHYNYL?)

FILE 'CAPLUS' ENTERED AT 16:28:14 ON 24 OCT 2002

L5 9 S L4

=> log y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION

FULL ESTIMATED COST

41.88	199.51
-------	--------

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

-5.58	-5.58
-------	-------

STN INTERNATIONAL LOGOFF AT 16:32:04 ON 24 OCT 2002